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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/669,833	09/26/2000	Linda S. Mansfield	MSU 4.1-528	2531

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/669,833	MANSFIELD ET AL	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment

1. Applicant's amendment filed on 9/8/03 is acknowledged.

Status of claims

2. Claims 29 and 30 have been amended.

Claims 29 and 30 are pending the application.

Claim Rejections - 35 USC 112, second paragraph withdrawn

3. In view of amendment to the claims, the rejection under 35 U.S.C. 112, second paragraph is withdrawn.

Claim Rejections - 35 USC 103 withdrawn

4. Upon further review of the application and arguments of record, the rejection under 35 U.S.C. 103(a) as being unpatentable over Liang et al 1998 or Marsh et al 1996 in view of Harlow and Lane 1988 is withdrawn.

New Claim Rejections - 35 USC 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30, step (b) is rejected as being vague and indefinite for the recitation of " providing a microorganism containing a DNA encoding a fusion polypeptide ----- (+/4) 16KD antigen and (+/- 4) 30 KD antigen." It is not clear which microorganism contains a DNA encoding which fusion polypeptide? Does fusion polypeptide contain 16KD antigen and 30 KD antigens? Or something else?

New Claim Rejections - 35 USC 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mora et al (Infect Immun. 1992 Aug; 60(8): 3442-5) in view of Liang et al 1998 (Infection and Immunity; 66 (5) 1834-1838) or Marsh et al 1996 (JAVMA, 209: 1907-1913).

Claim 29 is drawn to a method for producing an antibody against a Sarcocystis neurona antigen selected from the group consisting of 16 (+/-4) kD antigen and 30kD (+/-4) kDa antigen, as determined by SDS polyacrylamide gel electrophoresis, comprising: providing a Sarcocystis neurona antigen selected from the group consisting of the 16 (+/-4) kD antigen and the 30 (+/-4) kD antigen and admixing the antigen with an adjuvant to

produce an admixture to immunize a mammal to produce antibodies against antigen; removing serum from the immunized mammal and isolating from the serum the antibody.

Mora et al teach a method of making antibodies by inoculating rabbits (mammal) with C. parvum oocysts resuspended in complete Freund's adjuvant. Animals were bled and serum was obtained from immunized animals (see page 3442, right column through page 3443, left column). The serum antibodies are isolated on an immunoblot using C.parvum antigen (see figure 2). The teachings of Mora et al did not disclose immunizing animals with 16KD and 30 KD antigen of S.neurona.

However, Liang et al 1998 teach sera from infected horses with S.neurona specifically bind to 16KD and 30KD surface antigens of S.neurona (see figure 1 and page 1835, right column, first paragraph, figure 3 B, SDS-PAGE). Further, antibodies to 16KD antigen neutralized merozoites (see abstract and discussion). Liang suggests that antibodies to S.neurona 16KD antigen is a potential target for lysing the merozoites and thereby inhibit the infection (see Discussion). Thus the prior art suggests antibodies to 16KD are important surface antigen of S.neurona and could be used to inhibit infection.

Similarly, Marsh et al 1996 (JAVMA, 209: 1907-1913) teaches an immunodominant protein, approximately 29KD from S.neurona merozoites (see page 1910, left column and figure 3, SDA-PAGE). Marsh also suggests that specific antibodies to 30KD antigen would positively identify S.neurona infection from other infection because sera from infected horses not only contain antibodies to S.neurona but also antibodies to other parasitic infections and are cross reactive to 30KD antigen and thus resulted in false positive identification in western-blot analysis. Thus the teachings of Marsh et al suggested the importance of making antibodies against30KD antigen for use in specific diagnosis.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make antibodies to 16KD and 30 KD surface antigens of S.neurona using art known conventional methods of making antibodies as taught by Mora et al to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of overcoming or avoiding the problem of false positive results in diagnosing specific S.neurona infection from other parasitic infection as suggested by Marsh et al or for obtaining specific 16KD antibodies that are useful to inhibit merozoite infection in horses as suggested by Liang et al. The claimed invention is prima facie obvious over Mora et al in view of Liang et al or Marsh et al each absent any convincing evidence to the contrary.

9. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Avarzed et al Journal of Clinical Microbiology, July 1998, p. 1835-1839, Vol. 36, No. 7 in view of Liang et al 1998 (Infection and Immunity; 66 (5) 1834-1838) or Marsh et al 1996 (JAVMA, 209: 1907-1913).

Claim 30 is drawn to a method for producing a monoclonal antibody against a Sarcocystis neurona antigen selected from the group consisting of a 16 (+/-4) kDa antigen and a 30 (+/-4) kDa antigen, as determined SDS polyacrylamide gel electrophoresis, comprising: providing a microorganism containing a DNA encoding a fusion polypeptide which a Sarcocystis neurona antigen selected from the group consisting of the 16 (+/-4) kDa antigen and the 30 (+/-4) kDa antigen; admixing the antigen with an adjuvant to produce admixture; inoculating mice with the admixture to produce antibodies against antigen; removing the spleens from the mice which produce the antibodies against the antigen; removing spleen cells from the spleens and mixing the spleen cells from the spleens with mouse myeloma cells to produce a mixture

of fused cells consisting of spleen cells fused to myeloma cells, the spleen cells, and the myeloma cells; selecting the fused cells on cell culture medium in which the fused cells can grow but which the spleen cells and the myeloma cells cannot grow; and screening the fused cells for fused cells which produce the monoclonal antibody against the Sarcocystis neurona antigen selected from the group consisting of the 16 (+/-4) kDa antigen and the 30 (+/-4) kDa antigen to produce the monoclonal antibody.

Avarzed et al teach a method of producing MAb against B. equi to characterize the location of the protein for detecting the effect on parasite growth in vitro and to examine the potential application of species-specific protein of B. equi as an antigen in a serodiagnostic method (see page 1835, right column through page 1836, under Materials and Methods; see Production and purification of Mabs). The teachings of Avarzed et al have been explained above do not disclose immunizing animals with 16KD and 30 KD antigen of S.neurona to produce antibodies.

However, Liang et al 1998 teach sera from infected horses with S.neurona specifically bind to 16KD and 30KD surface antigens of S.neurona (see figure 1 and page 1835, right column, first paragraph, figure 3 B, SDS-PAGE). Further, antibodies to 16KD antigen neutralized merozoites (see abstract and discussion). Liang suggests that antibodies to S.neurona 16KD antigen are a potential target for lysing the merozoites and thereby inhibit the infection (see Discussion). Thus the prior art suggests antibodies to 16KD are important surface antigen of S.neurona and could be used to inhibit infection.

Similarly, Marsh et al 1996 (JAVMA, 209: 1907-1913) teach an immunodominant protein, approximately 29KD from S.neurona merozoites (see page 1910, left column and figure 3, SDA-PAGE). Marsh also suggests that specific antibodies to 30KD antigen would positively identify S.neurona infection from other infection because sera from

infected horses not only contain antibodies to S.neurona but also antibodies to other parasitic infections and are cross reactive to 30KD antigen and thus resulted in false positive identification in western-blot analysis. Thus the teachings of Marsh et al suggested the importance of making antibodies against30KD antigen for use in specific diagnosis.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make antibodies to 16KD and 30 KD surface antigens of S.neurona using art known conventional methods of making antibodies as taught by Avarzed et al to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of overcoming or avoiding the problem of false positive results in diagnosing specific S.neurona infection from other parasitic infection as suggested by Marsh et al or for making specific 16KD antibodies that are useful to inhibit merozoite infection in horses as suggested by Liang et al. The claimed invention is prima facie obvious over Avarzed et al in view of Liang et al or Marsh et al each, absent any convincing evidence to the contrary.

9. Claims 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harlow and Lane 1988 (Antibodies; Cold Spring Harbor) in view of Liang et al 1998 (Infection and Immunity; 66 (5) 1834-1838) or Marsh et al 1996 (JAVMA, 209: 1907-1913).

Claims have been described supra

It is conventional and routine in the art of immunology for methods of producing monoclonal antibodies and polyclonal antibodies against antigens, (Harlow and Lane chapter 6 and 5 respectively, 1988). The prior art teaches a method of producing antibodies by immunizing mice with antigen and adjuvant (see pages122, 123, 102,103,

106 from chapter 5). Further the prior art teaches a method of producing hyper-immune sera (see page 115 from chapter 5). Samples of blood were collected and serum-containing antibodies were isolated as described in page 119 from chapter 5 for checking the production of specific antibodies (page 116 from chapter 5).
The prior art also teaches method of producing monoclonal antibodies by immunizing mice with antigen and adjuvant (see page 148 from chapter 6) and spleen cells were removed and fused with myeloma cells. Fused cells were screened for the production of monoclonal antibodies (figures 6.1, 6.2, 6.3 and pages 148, 202, 217-219 from chapter 6). Thus the prior art teaches conventionally practiced methods of making antibodies using any antigen. The teachings of Harlow have been explained above which do not disclose immunizing animals with 16KD and 30 KD antigen of S.neurona.

However, Liang et al 1998 teach sera from infected horses with S.neurona specifically bind to 16KD and 30KD surface antigens of S.neurona (see figure 1 and page 1835, right column, first paragraph, figure 3 B, SDS-PAGE). Further, antibodies to 16KD antigen neutralized merozoites (see abstract and discussion). Liang suggests that antibodies to S.neurona 16KD antigen is a potential target for lysing the merozoites and thereby inhibit the infection (see Discussion). Thus the prior art suggests antibodies to 16KD are important surface antigen of S.neurona and could be used to inhibit infection.

Similarly, Marsh et al 1996 (JAVMA, 209: 1907-1913) teach an immunodominant protein, approximately 29KD from S.neurona merozoites (see page 1910, left column and figure 3, SDA-PAGE). Marsh also suggests that specific antibodies to 30KD antigen would positively identify S.neurona infection from other infection because sera from infected horses not only contain antibodies to S.neurona but also antibodies to other parasitic infections and are cross reactive to 30KD antigen and thus resulted in false

positive identification in western-blot analysis. Thus the teachings of Marsh et al suggested the importance of making antibodies against30KD antigen for use in specific diagnosis.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make antibodies to 16KD and 30 KD surface antigens of S.neurona using art known conventional methods of making antibodies as taught by Harlow et al to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of overcoming or avoiding the problem of false positive results in diagnosing specific S.neurona infection from other parasitic infection as suggested by Marsh et al or for making specific 16KD antibodies that are useful to inhibit merozoite infection in horses as suggested by Liang et al. The claimed invention is prima facie obvious over Harlow d et al in view of Liang et al or Marsh et al absent any convincing evidence to the contrary.

Remarks

10. Claims 29-30 are rejected.

Relevant Prior Art

11. The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

Letscher-Bru et al Infect Immun. 1998 Sep; 66(9): 4503-6 teach a method of producing antibodies by inoculating mice with recombinant Toxoplasma gondii surface antigen 1 (rSAG1) 30KD protein, alone or combined with interleukin-12 (IL-12) as an adjuvant in CBA/J mice (CERJ). rSAG1 protein expressed in *E. coli* . Mice were immunized twice a week for 2 weeks (days 1, 4, 8, and 13) with rSAG1 alone (cumulative dose, 4 µg) or with rSAG1 plus IL-12 (cumulative dose, 4 µg of each).

Bonnin et al Infect Immun. 1991 May; 59 (5): 1703–1708 teach method of making monoclonal antibodies (MAbs) against purified excysted oocysts and sporozoites of Cryptosporidium parvum reacted in an immunofluorescence assay with antigens located at the anterior pole of the mezoites. On Western blots of purified oocysts, these MAbs reacted with a series of bands between 210 and 40 kDa; several of these bands were recognized by both Mabs.

Conclusion

12. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.

6/6/04

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